

### REMARKS

The Applicants thank the Examiner for the examination to date and respectfully request reconsideration and allowance.

#### **Status of the claims:**

Claims 1-140 are pending. Claims 1, 2, 5, 7, 14, 17, 19, 21, 23-27, 34-41, 44, 46, 52, 55, 57, 59, 61-65, 71, 72, 80-85, 87-92, 94-103, 105-115, and 117-140 are rejected. The remaining claims are withdrawn.

The independent claims are 1, 40, 90, 100, 110, 111, 112, 120, 123, and 130.

The Applicants currently amend independent claim 1 but do not believe they introduce new matter. The phrases “layer” and “hydrophilic compound to inhibit protein adsorption” can be found in the filed application at, for example, working example one at page 22. See also amendment to independent claim 40.

In view of the large number of claims pending in the case, the Applicants provide a brief introduction. The Examiner has rejected most of the claims as anticipated over Mirkin. In addition, some claims are rejected as obvious, but Mirkin is still used as the primary reference in the obviousness rejections. The applicants, however, describe and claim improvements over Mirkin. Mirkin describes a lithographic process which can be used for a wide variety of patterning compounds including proteins. However, for commercial development of the Mirkin methods, improvements are desired for particular embodiments including proteins. For example, better reproducibility, faster deposition, and higher resolution can be commercially important. In this case, improved protein and peptide printing processes are desired, particularly proteins which are higher molecular weight materials which can diffuse more slowly from the tip to a surface and interact with the tip to resist deposition to the surface. The applicants have discovered commercially significant improvements to the protein and peptide printing processes which are not taught or suggested by Mirkin.

**Response to rejections under 35 USC §102(b)**

The examiner has rejected claims 1-2, 5, 7, 14, 17, 19, 21, 23-27, 34-35, 37-38, 40-41, 44, 46, 52, 55, 57, 59, 61-65, 71-72, 80-81, 84, 87, 90, 91-92, 94-96, 98-102, 110-115, 117-132, 134-135, and 137-140 under 102(b) as anticipated by Mirkin et al (WO00/41213). The applicants respectfully traverse.

**1. Independent claim 1 and claims dependent thereon**

Claim 1 as filed is not anticipated by Mirkin because Mirkin does not describe that the tip is modified by a selected chemical agent to improve deposition of the selected protein patterning compound to the substrate surface. Mirkin generally describes tip modification with use of an adhesion layer, tip cleaning, or tip etching at page 6, line 29 to page 7, line 25. However, this teaching does not result in anticipation. The Mirkin teaching focuses on adapting the tip modification with the solvent selection. The teaching does not focus on adapting the tip modification with a selected chemical agent and with the selected protein patterning compound.

To increase the distance between the prior art and the claim, however, the applicants herein amend the claim to recite “selected hydrophilic compound” rather than “selected chemical agent.” Mirkin does not describe use of a selected hydrophilic compound. Moreover, claim 1 is amended to recite that the tip is modified to inhibit protein adsorption which Mirkin does not teach. Hence, no anticipation is present.

The Examiner refers to Mirkin’s teaching of modifying tips with a hydrophobic compound and appears also to suggest incorrectly that polyethylene glycol is a hydrophobic compound (office action, page 3). The applicants respectfully traverse. Polyethylene glycol is a water soluble, hydrophilic material, not a hydrophobic material. Moreover, Mirkin teaches use of hydrophobic tip modification for improved AFM imaging, whereas the present claims focus on deposition, not imaging.

If the Examiner chooses to rely on inherency theory to support an anticipation argument, the Examiner should provide a technically cogent argument to support the assertion. For example, while Mirkin teaches use of titanium adhesion layers, cleaning tips, and etching tips,

Mirkin does not suggest that these steps specifically improve protein deposition or inhibit protein adsorption.

In sum, Mirkin does not anticipate claim 1.

The Examiner has not rejected claim 1 as obvious over Mirkin or any other prior art, but the applicants briefly note obviousness. The subject matter of claim 1 would also have been non-obvious over Mirkin. While Mirkin describes generally deposition of a wide variety of patterning compounds, including proteins, Mirkin does not address specific problems and improvements associated with a commercial process for protein deposition, particularly issues such as reproducibility and patterning speed. The technology described in Mirkin and presently claimed can be subtly complex because one needs to find a way initially to get the deposition material onto the tip, and then subsequently transfer that same material off of the tip. These issues can be made more difficult with higher molecular weight materials such as proteins, because transport of compound from tip to surface can be regulated in part by diffusion, and diffusion processes are generally slower for larger molecular weight compounds such as proteins. Mirkin does not address the particular issues found with proteins.

Mirkin teaches that tip modification can be carried out so that physical adsorption of the patterning compound to the tip is enhanced. The applicants claim that adsorption results in inhibition of the protein adsorption. Hence, Mirkin teaches away.

In this context, the claimed subject matter would not have been obvious. The presently claimed subject matter provides a patentable improvement over Mirkin making the Mirkin process more commercially useful.

2. Independent claim 40 and claims dependent thereon.

Independent claim 40 is also rejected as anticipated over Mirkin. Claim 40, however, also recites the hydrophilic compound, and the applicants assert that Mirkin does not anticipate or render obvious the subject matter of claim 40, both before and after the present amendment.

3. Independent claim 90 and claims dependent thereon.

Regarding claim 90, the Examiner alleges that “Mirkin teaches silicon nitride tips coated with titanium.” (office action, page 4). Claim 90 recites providing an AFM tip “modified to resist protein adsorption and which is coated with protein,” and “providing a substrate comprising an electrostatically charged surface.” However, the examiner does not provide specific facts to show that each limitation of independent claim 90 is taught by Mirkin. Mirkin does not appear to teach or suggest an electrostatically charged surface. Mirkin’s approach utilizes chemisorption and covalent bonding in contrast to electrostatic. Mirkin teaches tip modification to enhance physisorption of the patterning compound to the tip. Claim 90 recites a different concept: modification to resist protein adsorption.

4. Independent claim 100 and claims dependent thereon.

Regarding claim 100, the Examiner merely alleges that “Mirkin teaches silicon nitride tips coated with titanium.” (office action, page 4). Claim 100 recites “the tip comprises a **metallic surface** which has been **treated** to promote protein or peptide coating ...” The examiner fails to show that Mirkin teaches that in addition to a tip comprising a metallic surface, the surface has been treated and the treatment promotes protein or peptide coating. Therefore, claim 100 is not anticipated by Mirkin.

Claims 101-102, dependents of claim 100, are therefore not anticipated by Mirkin.

5. Regarding amended claims 110 and 111, because Mirkin does not teach that a tip is modified by a hydrophilic biocompatible compound to improve the deposition of selected protein or peptide patterning compound to the substrate surface, they are not anticipated by Mirkin.

6. Regarding claims 112, the Examiner alleges that “Mirkin teaches an array of 0.46 $\mu$ m diameter dots, each dot being separated by 0.54  $\mu$ m. See page 21, line 20-26.” (OA page 4). The cited part is directed to ODT (octadecanethiol) dots, whereas claim 112 is directed to protein and peptide arrays. Therefore, Mirkin does not teach the invention in claim 112.

Because claims 113, 114, 115, 117, 118 and 119 are dependent of claim 112, they are not anticipated by Mirkin as well.

7. Regarding claim 120, the examiner alleges that “Mirkin teaches a separation distance of 70nm. See page 6, lines 6-7.” (OA, Page 5). The cited part is directed to a pattern generated with MHA (1,16-mercaptohexadecanoic acid) molecules by DPN. (Mirkin, Page 6, Lines 1-7), whereas claim 120 is directed to a plurality of different protein nanoscopic deposits. Because Mirkin does not teach each and every limitation, claim 120 is not anticipated by Mirkin.

Because claims 121 and 122 are dependent claim of claim 120, they are not anticipated by Mirkin as well.

8. Regarding claim 123, the examiner alleges that “Mirkin teaches printing an array of 25 dots in 20 seconds. See page 21, lines 20-23.” The cited part is directed to an array of ODT (octadecanethiol) dots generated by an ODT-coated tip. (Mirkin, Page 21, line 20-23). Claim 123 is directed to a protein array of protein dots. Because Mirkin does not teach each and every limitation, claim 123 is not anticipated by Mirkin.

Because claims 124-129 are dependent claim of claim 123, they are not anticipated by Mirkin as well.

9. Regarding claim 130, the examiner alleges that “Mirkin teaches an array of 0.46  $\mu\text{m}$  diameter dots, each being separated by 0.54  $\mu\text{m}$ . See page 21, line 20-26.” Again, the cited part is directed to an array of ODT (octadecanethiol) dots generated by an ODT-coated tip. (Mirkin, Page 21, line 20-26), whereas claim 130 is directed to a protein array of a plurality of protein dots. Because Mirkin does not teach each and every limitation, claim 130 is not anticipated by Mirkin.

10. Regarding claim 131-132, the examiner alleges that “Mirkin teaches dot diameter of 15 nm. See page 5, lines 25-26.” (OA page 5) The cited part is directed to an array of MHA

(1,16-mercaptohexadecanoic acid) dots generated by an MHA-coated tip. (Mirkin, Page 5, line 25-26), whereas claims 131-132 are directed to a protein array of a plurality of protein dots. Because Mirkin does not teach each and every limitation, claim 130 is not anticipated by Mirkin.

Because claims 133-137 are dependent claims of claim 130, they are not anticipated by Mirkin as well.

**Response to rejections under 35 USC §103(a):**

1. Claims 36, 39, 82-83, 85, and 88-89 are rejected under 103(a) as being unpatentable over Mirkin (WO 00/41213).

Arguments already asserted and amendments made to claims 1 and 40 render moot the obviousness rejections.

To establish a *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. Because Mirkin does not teach all the claim limitations, the Examiner fails to establish a *prima facie* obviousness of claim 36, 39, 82-83, 85, and 88-89.

Regarding claims 36 and 38, which are dependent of claim 1, Mirkin does not teach a tip modified by a hydrophilic biocompatible compound. Therefore, rejections of claims 36 and 38 as being obvious are moot.

Regarding claims 82-83, 85, and 88-89, which are dependent of claim 40, Mirkin does not teach a tip modified by a hydrophilic biocompatible compound. Therefore, rejections of the claim as being obvious are moot.

2. Claims 97 and 103 are rejected under §103(a) as being unpatentable over Mirkin (WO 00/41213) in view of Duffy (US 2002/0028463 A1).

Regarding claim 97, which is dependent of claim 90, Mirkin does not teach “providing an atomic force microscopic tip modified to resist protein adsorption and which is coated with

protein,” and “providing a substrate comprising an electrostatically charged surface.” Therefore, Mirkin and Duffy together do not teach all the claim limitations.

Regarding claim 103, which is dependent of claim 100, Mirkin does not teach “a metallic surface which has been treated to promote protein or peptide coating of the tip.” Therefore, Mirkin and Duffy together do not teach all the claim limitations.

For the reasons noted above, the examiner fails to establish a *prima facie* obviousness of claim 97. Therefore, rejections of claims 97 and 103 for being obvious are improper.

3. Claims 105, 107-108 are rejected under §103(a) as being unpatentable over Mirkin (WO 00/41213) in view of Majumdar (US 2002/0102743 A1).

Claims 105 and 107-108 are dependent of claim 100. For the same reason set forth above regarding claim 103, Mirkin and Majumdar together do not teach all the claim limitations.

4. Claims 106 and 136 are rejected under §103(a) as being unpatentable over Mirkin (WO 00/41213) in view of Everhart (US 2001/0004526 A1).

Regarding claim 106, the examiner alleges that “..., Mirkin also teaches that the substrate can be any material, including metals such as gold. See page 7, line 26 to page 8, line 20.” In claim 106, the surface (per claim 100) refers to **tip’s metallic surface** whereas the cited part teaches a **substrate surface**. Therefore, the facts and reasons are misplaced. Thus Mirkin and Everhart together do not teach all the claim limitations.

Regarding claim 136, the examiner has not provided any facts or reasons in making the rejection. The applicants respectfully invite the examiner to provide such facts or reasons.

For the reasons set forth above, the Examiner has not established a *prima facie* obviousness of claims 106 and 136.

5. Claims 109 is rejected under §103(a) as being unpatentable over Mirkin (WO 00/41213) in view of Majumdar (US 2002/0102743 A1).

Regarding claim 109, the examiner alleges that "...and Mirkin also teaches that relative humidity affects....See page 17, line 13-18." The cited part is directed to deposition of ODT as patterning compound on substrate surface, whereas, claim 109 is directed to deposition of protein or peptide. Furthermore, Mirkin does not teach a tip "comprises a metallic surface which has been treated to promote..." The examiner has not provided facts or reasons as to whether Majumbar teaches any missing limitations not taught by Mirkin. Thus Mirkin and Majumdar together do not teach all the claim limitations. For the reasons set forth above, the Examiner has not established a *prima facie* obviousness of claim 109, therefore the rejections are improper.

6. Claim 133 rejected under §103(a) as being unpatentable over Mirkin (WO 00/41213).

Regarding claim 133 which is dependent of claim 130, as the applicants point out earlier, Mirkin does not teach all claim limitations of claim 130, therefore Mirkin does not teach all the claim limitations of claim 133. For the reasons set forth above, the Examiner has not established a *prima facie* obviousness of claim 133.

**Response to double-patenting rejection under 35 USC §101:**

The examiner has provisionally rejected claims 1-2, 5, 7, 14, 17, 19, 21, 23-27, 34-36, 37-41, 44, 46, 52, 55, 57, 59, 61-65, 71-72, 80-85, 87-92, 94-103, 105-115. and 117-140 over application no. 10/442,189, which is a parent to the present case. The applicants stress that application no. 10/442,189 is presently abandoned. Therefore, the double patenting rejection is moot.

**Conclusion:**

For the reasons set forth above, the pending claims are not anticipated or rendered obvious by the cited art.

The applicants believe that the pending claims are now in condition for allowance. Accordingly, they request favorable consideration of the application as amended. The examiner



is kindly invited to contact the undersigned by telephone if a telephone interview would advance the prosecution efficiently.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or in formal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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